

***Remarks***

***Status of the Claims***

Claims 1-3, 5-23, 26, 28-31, 33, 35, 37-39, 44-47, 54, 55, 57 and 59 are pending in the application, with claims 1-3, 30 and 31 being the independent claims. Claims 24, 25, 27, 36, 48-53, 56 and 58 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein. Claims 1, 2, 3, 5, 6, 8, 10, 12, 14, 16, 18, 20, 30, 31, 37, 54, 55, 57 and 59 are sought to be amended. Support for the amendments to claims 1, 2, 3, 30 and 31 may be found throughout the specification, for example at page 17, lines 18-31, page 18, lines 1-2 and in the original claims. Other amendments incorporate features recited in canceled claims or change claim dependencies. No new matter is added by these amendments, and their entry and consideration are respectfully requested.

***Rejection Under 35 U.S.C. § 112, First Paragraph***

Claims 5-23 and 25 were rejected under 35 U.S.C. § 112, first paragraph, for failing to comply with the written description requirement. Office Action, pages 2-5. By the foregoing amendments, claim 25 has been cancelled, thus rendering moot the portion of this rejection that may have applied to that claim. Applicants respectfully traverse this rejection as it may apply to the remaining claims.

The Office Action states that “these compositions comprise an extremely large number of mutant DNA polymerases, which the specification does not describe, and also includes mutant polymerases that have not been taught in either the specification *or* the art.” Office Action at page 3. Applicants maintain that claims directed to mutant DNA polymerases are fully supported by the specification, but nonetheless have amended claims 5, 6, 8, 10, 12, 14, 16, 18 and 20 to delete reference to “mutants” to advance prosecution of the

application and not in acquiescence to this rejection. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, are respectfully requested.

***Rejections under 35 U.S.C. § 102(b)***

***A. The Rejection over Scalice.*** Claims 1, 44, 48, and 53-54 were rejected under 35 U.S.C. § 102(b) as being anticipated by Scalice *et al.* (U.S. Patent No. 5,338,671). Claims 48 and 53 are sought to be cancelled without prejudice or disclaimer, so the rejection of these claims is moot. Applicants respectfully traverse this rejection with respect to remaining claims 1, 44 and 54.

Claims 1, 44 and 54 relate to compositions for nucleic acid manipulations, in which the reagents are at concentrations for performing the methods ***without dilution***. In contrast, Scalice discloses a ***2.5X concentrate*** that ***is diluted*** prior to use. The reagents in the Scalice composition are not at a concentration for performing the intended nucleic acid manipulations without dilution. Rather, the Scalice composition ***is diluted*** prior to use, and therefore does not anticipate claims 1, 44 and 54. Applicants therefore respectfully request that the rejection of these claims under 35 U.S.C. § 102(b) over Scalice be reconsidered and withdrawn.

***B. The Rejection over Vizard.*** Claims 1-3, 5, 8, 24-28, 30, 31, 35, and 48-59 were rejected under 35 U.S.C. § 102(b) as being anticipated by Vizard *et al.* (WO 90/08839). Claims 24, 25, 27, 48-53, 56 and 58 are sought to be cancelled without prejudice or disclaimer, so the rejection of these claims is moot. Applicants respectfully traverse this rejection with respect to remaining claims 1-3, 5, 8, 26, 28, 30, 31, 35, 54, 55, 57 and 59.

Claims 1-3, 5, 8, 26, 28, 30, 31, 35, 54, 55, 57 and 59 relate to compositions, kits and methods for nucleic acid manipulations, in which the reagents are at concentrations for

performing the methods *without dilution*. In contrast, Vizard discloses “a nucleotide sequencing reaction *concentrate*” (Vizard at page 3, lines 22-23 (emphasis added)) that *is diluted* prior to use. The reagents in the Vizard composition are not at concentrations for performing the intended nucleic acid manipulations without dilution. Rather, the Vizard composition *is diluted* prior to use, and therefore does not anticipate claims 1-3, 5, 8, 26, 28, 03, 31, 35, 54, 55, 57 and 59. Applicants therefore respectfully request that the rejection of these claims under 35 U.S.C. § 102(b) over Vizard be reconsidered and withdrawn.

### *Rejections under 35 U.S.C. § 103*

The pending claims were rejected under 35 U.S.C. § 103(a) as being unpatentable over various combinations of the following references: Vizard et al. (WO90/08839); Soderlund et al. (EP 0648280); Lundberg et al. (*Gene* 108:1-6, 1991); Sobol et al. (U.S. 5,543,296); Isner (U.S. Pat. No. 5,652,225); Hughes et al. (WO96/10640); Scalice (U.S. Pat. No. 5,338,671); Barnes et al. (*Proc. Natl. Acad. Sci. U.S.A.* 91:2216-2220, 1994), Gelfand et al. (U.S. 5,420,029); Hinnisdaels et al. (*Biotechniques* 20:186-188, 1996); and Heath et al. (*Nucl. Acids Res.* 21:5782-5785, 1993). Not one of the cited combinations of references teaches or suggests compositions, kits or methods for nucleic acid manipulation that involve:

1. a nonionic detergent;
2. reagents, at concentrations for performing the methods without dilution;
3. a thermostable enzyme / polymerase which retains at least 90% of enzymatic activity for at least 4 weeks when stored at about 20-25°C; and
4. no nucleic acids.

As discussed below, none of the combinations of references set forth in the various rejections under 35 U.S.C. § 103 teaches or suggests all of these unique features.

Establishing *prima facie* obviousness requires a showing that each claim element is taught or suggested by the prior art. *See In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Specifically, establishing *prima facie* obviousness requires a showing that some combination of objective teachings in the art and / or knowledge available to one of skill in the art would have lead that individual to arrive at the claimed invention. *See In re Fine*, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988). Moreover, establishing *prima facie* obviousness requires not only that such a combination of prior art teachings is possible, but also that the teachings would have (a) motivated the skilled artisan to make the combination to arrive at the claimed invention, and (b) suggested to the skilled artisan a reasonable likelihood of success in making and using the claimed invention. *See In re Dow Chem. Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988). Absent a showing of such motivation and suggestion, *prima facie* obviousness is not established. *See In re Fine*, 5 USPQ2d at 1598.

The Court of Appeals for the Federal Circuit specifically held in *Tec-Air, Inc. v. Dense Manufacturing Michigan Inc.*, 192 F.3d 1353 (Fed. Cir. 1999), that:

There is no suggestion to combine... if a reference teaches away from its combination with another source.' ... A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant . . . [or] if it suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought by the applicant.' *In re Gurley* . . . (Fed. Cir. 1994).

The Federal Circuit further held that "references that teach away cannot serve to create a *prima facie* case of obviousness," *In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994), and that an "applicant may rebut a *prima facie* case of obviousness by showing that the prior art teaches away from the claimed invention in any material respect." *In re Geisler*, 116 F.3d 1465, 1469 (Fed. Cir. 1997).

***A. The rejection over Vizard in view of Soderlund***

Claim 29 was rejected under 35 U.S.C. § 103(a) over Vizard in view of Soderlund. Applicants respectfully traverse.

A *prima facie* case of obviousness of claim 29 over Vizard in view of Soderlund has not been established. Nothing in the Vizard or Soderlund references would have motivated the skilled artisan to combine them to arrive at the claimed invention. If anything, the cited references teach away from the claimed invention. As was the case in *Tec-Air*, the skilled artisan reading the cited references “would be led in a direction divergent from the path that was taken by the applicant.”

Claim 29 relates to compositions for nucleic acid manipulations, in which the reagents are at concentrations for performing the methods ***without dilution***. In complete and total contrast, Vizard discloses “a nucleotide sequencing reaction ***concentrate***” that ***is diluted*** prior to use. The reagents in the Vizard composition are not at concentrations for performing the intended nucleic acid manipulations without dilution. Rather, the Vizard composition ***is diluted*** prior to use. Vizard’s dilution approach is 180 degrees different from the claimed invention. As was the case in *Tec-Air*, the cited reference teaches away from the claimed invention; the skilled artisan reading Vizard “would be led in a direction divergent from the path that was taken by the applicant.”

Vizard clearly teaches away from the claimed invention, and in accord with the Federal Circuit’s guidance in *In re Gurley*, cannot serve to create a *prima facie* case of obviousness. Because nothing in Vizard or Soderlund would have motivated the skilled artisan to combine these references to arrive at the claimed invention, and because Vizard actually teaches away from the claimed invention, a *prima facie* showing of obviousness

cannot be properly be maintained. Applicants therefore respectfully request that the Examiner reconsider and withdraw the rejection of claim 29 under 35 U.S.C. §103(a).

***B. The rejection over Sorge in view of Slatko***

Claim 36 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Sorge in view of Slatko. Although Applicants maintain their traversal of this rejection for reasons provided in their response filed April 5, 2004, claim 36 has been canceled without prejudice in an earnest effort to advance prosecution of the application, and not in acquiescence to this rejection which has nonetheless been rendered moot.

***C. The rejection over Lundberg in view of Sobol, Isner and Vizard***

Claims 1-2, 5, 6, 8-9, 18, 19, 24-28, 30, 33, 48, 49, and 53-55 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Lundberg in view of Sobol, Isner and Vizard. Claims 24, 25, 27, 48, 49 and 53 are sought to be cancelled without prejudice or disclaimer, so the rejection of these claims is moot. Applicants respectfully traverse this rejection with respect to remaining claims 1-2, 5, 6, 8-9, 18, 19, 26, 28, 30, 33, 54 and 55.

A *prima facie* case of obviousness of claims 1-2, 5, 6, 8-9, 18, 19, 26, 28, 30, 33, 54 and 55 over Lundberg in view of Sobol, Isner and Vizard has not been established. Nothing in these references would have motivated the skilled artisan to combine them to arrive at the claimed invention.

Claims 1-2, 5, 6, 8-9, 18, 19, 26, 28, 30, 33, 54 and 55 relate to compositions and kits for nucleic acid manipulations, in which the reagents are at concentrations for performing the methods *without dilution*. Vizard discloses *concentrates that are diluted* prior to use. Thus,

Vizard clearly teaches away from the present invention and cannot serve to create a *prima facie* case of obviousness.

In addition, claims 1-2, 5, 6, 8-9, 18, 19, 26, 28, 30, 33, 54 and 55 relate to compositions that ***lack nucleic acids*** and that can be stored for later use. These features allow the claimed invention to be used by many researchers to manipulate any desired nucleic acids. In complete and total contrast, Lundberg and Isner disclose compositions that ***contain nucleic acids*** for immediate manipulation in their specific research. This approach totally impairs the flexibility of the claimed invention, which can be used by many researchers to manipulate any desired nucleic acid. Thus, the approach taken by Lundberg and Isner is 180 degrees different from the claimed invention. The skilled artisan reading these references “would be led in a direction divergent from the path that was taken by the applicant.” Lundberg and Isner clearly teach away from the claimed invention, and in accord with the Federal Circuit’s guidance in *In re Gurley* cannot serve to create a *prima facie* case of obviousness. Because nothing in Lundberg or Isner would have motivated the skilled artisan to combine these references to arrive at the claimed invention, and because these references actually teach away from the claimed invention, a *prima facie* showing of obviousness cannot be properly be maintained.

The remaining reference (*i.e.* Sobol) does not teach or suggest compositions for nucleic acid manipulation that comprise:

1. a nonionic detergent;
2. reagents, at concentrations for performing the methods without dilution;
3. a thermostable enzyme / polymerase which retains at least 90% of enzymatic activity for at least 4 weeks when stored at about 20-25°C; and
4. no nucleic acids.

Applicants therefore respectfully request that the rejection of claims 1-2, 5, 6, 8-9, 18, 19, 26, 28, 30, 33, 54 and 55 under 35 U.S.C. §103(a) over Lundberg in view of Sobol, Isner and Vizard be reconsidered and withdrawn.

***D. The rejection over Lundberg in view of Sobol, Isner, Vizard and Hughes***

Claims 10 and 11 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Lundberg in view of Sobol, Isner, Vizard and Hughes. Applicants respectfully traverse this rejection.

A *prima facie* case of obviousness of claims 10 and 11 over Lundberg in view of Sobol, Isner, Vizard and Hughes has not been established. Nothing in these references would have motivated the skilled artisan to combine them to arrive at the claimed invention.

Claims 10 and 11 relate to compositions for nucleic acid manipulations, in which the reagents are at concentrations for performing the methods ***without dilution***. Vizard discloses ***concentrates that are diluted*** prior to use. Thus, Vizard clearly teaches away from the present invention and cannot serve to create a *prima facie* case of obviousness.

In addition, claims 10 and 11 relate to compositions that ***lack nucleic acids*** and that can be stored for later use. Isner and Hughes teach compositions that ***contain nucleic acid*** for immediate manipulation in their specific research. Thus, Isner and Hughes clearly teach away from the claimed invention and cannot serve to create a *prima facie* case of obviousness.

The remaining reference (*i.e.* Sobol) does not teach or suggest compositions for nucleic acid manipulation that comprise:

1. a nonionic detergent;
2. reagents, at concentrations for performing the methods without dilution;



3. a thermostable enzyme / polymerase which retains at least 90% of enzymatic activity for at least 4 weeks when stored at about 20-25°C; and
4. no nucleic acids.

Applicants therefore respectfully request that the rejection of claims 10 and 11 under 35 U.S.C. §103(a) over Lundberg in view of Sobol, Isner, Vizard and Hughes be reconsidered and withdrawn.

***E. The rejection over Hughes in view of Lundberg, Sobol, Isner and Vizard***

Claims 1-2, 5, 6, 8-11, 18, 19, 24-28, 30, 33, 48, 49, and 53-55 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Hughes in view of Lundberg, Sobol, Isner and Vizard. Claims 24, 25, 27, 48, 49 and 53 are sought to be cancelled without prejudice or disclaimer, so the rejection of these claims is moot. Applicants respectfully traverse this rejection with respect to remaining claims 1-2, 5, 6, 8-11, 18, 19, 26, 28, 30, 33, 54 and 55.

A *prima facie* case of obviousness of claims 1-2, 5, 6, 8-11, 18, 19, 26, 28, 30, 33, 54 and 55 over Hughes in view of Lundberg, Sobol, Isner and Vizard has not been established. Nothing in these references would have motivated the skilled artisan to combine them to arrive at the claimed invention.

Claims 1-2, 5, 6, 8-11, 18, 19, 26, 28, 30, 33, 54 and 55 relate to compositions and kits for nucleic acid manipulations, in which the reagents are at concentrations for performing the methods *without dilution*. Vizard discloses *concentrates that are diluted* prior to use. Thus, Vizard clearly teaches away from the present invention and cannot serve to create a *prima facie* case of obviousness.

In addition, claims 1-2, 5, 6, 8-11, 18, 19, 26, 28, 30, 33, 54 and 55 relate to compositions that *lack nucleic acids* and that can be stored for later use. Hughes, Lundberg

and Isner teach compositions that *contain nucleic acid* for immediate manipulation in their specific research. Thus, Hughes, Lundberg and Isner clearly teach away from the claimed invention and cannot serve to create a *prima facie* case of obviousness.

The remaining reference (i.e. Sobol) does not teach or suggest compositions for nucleic acid manipulation that comprise:

1. a nonionic detergent;
2. reagents, at concentrations for performing the methods without dilution;
3. a thermostable enzyme / polymerase which retains at least 90% of enzymatic activity for at least 4 weeks when stored at about 20-25°C; and
4. no nucleic acids.

Applicants therefore respectfully request that the rejection of claims 1-2, 5, 6, 8-11, 18, 19, 26, 28, 30, 33, 54 and 55 under 35 U.S.C. §103(a) over Hughes in view of Lundberg, Sobol, Isner and Vizard be reconsidered and withdrawn.

***F. The rejection over Scalice et al. in view of Sobol, Isner and Vizard***

Claims 2, 5, 6, 8, 18, 24-28, 30, 33, 45-47, 49, 51, and 55-57 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Scalice in view of Sobol, Isner and Vizard. Claims 24, 25, 27, 49, 51 and 56 are sought to be cancelled without prejudice or disclaimer, so the rejection of these claims is moot. Applicants respectfully traverse this rejection with respect to remaining claims 2, 5, 6, 8, 18, 26, 28, 30, 33, 45-47, 55 and 57.

A *prima facie* case of obviousness of claims 2, 5, 6, 8, 18, 26, 28, 30, 33, 45-47, 55 and 57 over Scalice in view of Sobol, Isner and Vizard has not been established. Nothing in these references would have motivated the skilled artisan to combine them to arrive at the claimed invention.

Claims 2, 5, 6, 8, 18, 26, 28, 30, 33, 45-47, 55 and 57 relate to compositions and kits for nucleic acid manipulations, in which the reagents are at concentrations for performing the methods *without dilution*. Vizard and Scalice disclose *concentrates that are diluted* prior to use. Thus, Vizard and Scalice clearly teach away from the present invention and cannot serve to create a *prima facie* case of obviousness.

In addition, claims 2, 5, 6, 8, 18, 26, 28, 30, 33, 45-47, 55 and 57 relate to compositions that *lack nucleic acids* and that can be stored for later use. Isner discloses compositions that *contain nucleic acids* for immediate manipulation in their specific research. Thus, Isner clearly teaches away from the claimed invention and cannot serve to create a *prima facie* case of obviousness.

The remaining reference (i.e. Sobol) does not teach or suggest compositions for nucleic acid manipulation that comprise:

1. a nonionic detergent;
2. reagents, at concentrations for performing the methods without dilution;
3. a thermostable enzyme / polymerase which retains at least 90% of enzymatic activity for at least 4 weeks when stored at about 20-25°C; and
4. no nucleic acids.

Applicants therefore respectfully request that the rejection of claims 2, 5, 6, 8, 18, 26, 28, 30, 33, 45-47, 55 and 57 under 35 U.S.C. §103(a) over Scalice in view of Sobol, Isner and Vizard be reconsidered and withdrawn.

***G. The rejection over Barnes in view of Sobol, Isner and Vizard***

Claims 1-2, 5-9, 14-19, 22-26, 28, 33, 37-43, and 48-49 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Barnes in view of Sobol, Isner, and Vizard. Claims 40-

43 were previously cancelled, and claims 24, 25, 48 and 49 are sought to be cancelled without prejudice or disclaimer, so the rejection of these claims is moot. Applicants respectfully traverse this rejection with respect to remaining claims 1-2, 5-9, 14-19, 22, 23, 26, 28, 33 and 37-39.

A *prima facie* case of obviousness of claims 1-2, 5-9, 14-19, 22, 23, 26, 28, 33 and 37-39 over Barnes in view of Sobol, Isner and Vizard has not been established. Nothing in these references would have motivated the skilled artisan to combine them to arrive at the claimed invention.

Claims 1-2, 5-9, 14-19, 22, 23, 26, 28, 33 and 37-39 relate to compositions and methods for nucleic acid manipulations, in which the reagents are at concentrations for performing the methods *without dilution*, and wherein the composition has no nucleic acid molecules. Vizard discloses *concentrates that are diluted* prior to use. Thus, Vizard clearly teaches away from the present invention and cannot serve to create a *prima facie* case of obviousness.

In addition, claims 1-2, 5-9, 14-19, 22, 23, 26, 28, 33 and 37-39 relate to compositions that *lack nucleic acids* and that can be stored for later use. Barnes and Isner disclose compositions that *contain nucleic acids* for immediate manipulation in their specific research. Thus, Barnes and Isner clearly teach away from the claimed invention and cannot serve to create a *prima facie* case of obviousness.

The remaining reference (i.e. Sobol) does not teach or suggest compositions for nucleic acid manipulation that comprise:

1. a nonionic detergent;
2. reagents, at concentrations for performing the methods without dilution;

3. a thermostable enzyme / polymerase which retains at least 90% of enzymatic activity for at least 4 weeks when stored at about 20-25°C; and
4. no nucleic acids.

Applicants therefore respectfully request that the rejection of claims 1-2, 5-9, 14-19, 22, 23, 26, 28, 33 and 37-39 under 35 U.S.C. §103(a) over Barnes in view of Sobol, Isner and Vizard be reconsidered and withdrawn.

***H. The rejection over Gelfand in view of Sobol, Isner and Vizard***

Claims 1-2, 5, 12, 13, 24-26, 33, 40, and 48-49 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Gelfand in view of Sobol, Isner and Vizard. Claim 40 was previously cancelled, and claims 24, 25, 48 and 49 are sought to be cancelled without prejudice or disclaimer, so the rejection of these claims is moot. Applicants respectfully traverse this rejection with respect to remaining claims 1-2, 5, 12, 13, 26 and 33.

A *prima facie* case of obviousness of claims 1-2, 5, 12, 13, 26 and 33 over Gelfand in view of Sobol, Isner and Vizard has not been established. Nothing in these references would have motivated the skilled artisan to combine them to arrive at the claimed invention.

Claims 1-2, 5, 12, 13, 26 and 33 relate to compositions for nucleic acid manipulations, in which the reagents are at concentrations for performing the methods ***without dilution***, and wherein the composition has no nucleic acid molecules. Vizard discloses ***concentrates that are diluted*** prior to use. Thus, Vizard clearly teaches away from the present invention and cannot serve to create a *prima facie* case of obviousness.

In addition, claims 1-2, 5, 12, 13, 26 and 33 relate to compositions that ***lack nucleic acids*** and that can be stored for later use. Gelfand and Isner disclose compositions that ***contain nucleic acids*** for immediate manipulation in their specific research. Thus, Gelfand

and Isner clearly teach away from the claimed invention and cannot serve to create a *prima facie* case of obviousness.

The remaining reference (i.e. Sobol) does not teach or suggest compositions for nucleic acid manipulation that comprise:

1. a nonionic detergent;
2. reagents, at concentrations for performing the methods without dilution;
3. a thermostable enzyme / polymerase which retains at least 90% of enzymatic activity for at least 4 weeks when stored at about 20-25°C; and
4. no nucleic acids.

Applicants therefore respectfully request that the rejection of claims 1-2, 5, 12, 13, 26 and 33 under 35 U.S.C. §103(a) over Gelfand in view of Sobol, Isner and Vizard be reconsidered and withdrawn.

***I. Rejection over Hinnisdaels in view of Sobol, Isner and Vizard***

Claims 1-2, 6, 20, 24-26, 28, 33, 40, and 48-49 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Hinnisdaels in view of Sobol, Isner and Vizard. Claim 40 was previously cancelled, and claims 24, 25, 48 and 49 are sought to be cancelled without prejudice or disclaimer, so the rejection of these claims is moot. Applicants respectfully traverse this rejection with respect to remaining claims 1-2, 6, 20, 26, 28 and 33.

A *prima facie* case of obviousness of claims 1-2, 6, 20, 26, 28 and 33 over Hinnisdaels in view of Sobol, Isner and Vizard has not been established. Nothing in these references would have motivated the skilled artisan to combine them to arrive at the claimed invention.

Claims 1-2, 6, 20, 26, 28 and 33 relate to compositions for nucleic acid manipulations, in which the reagents are at concentrations for performing the methods *without dilution*, and wherein the composition has no nucleic acid molecules. Vizard discloses *concentrates that are diluted* prior to use. Thus, Vizard clearly teaches away from the present invention and cannot serve to create a *prima facie* case of obviousness.

In addition, claims 1-2, 6, 20, 26, 28 and 33 relate to compositions that *lack nucleic acids* and that can be stored for later use. Hinnisdaels and Isner disclose compositions that *contain nucleic acids* for immediate manipulation in their specific research. Thus, Hinnisdaels and Isner clearly teach away from the claimed invention and cannot serve to create a *prima facie* case of obviousness.

The remaining reference (i.e. Sobol) does not teach or suggest compositions for nucleic acid manipulation that comprise:

1. a nonionic detergent;
2. reagents, at concentrations for performing the methods without dilution;
3. a thermostable enzyme / polymerase which retains at least 90% of enzymatic activity for at least 4 weeks when stored at about 20-25°C; and
4. no nucleic acids.

Applicants therefore respectfully request that the rejection of claims 1-2, 6, 20, 26, 28 and 33 under 35 U.S.C. §103(a) over Hinnisdaels in view of Sobol, Isner and Vizard be reconsidered and withdrawn.

***J. Rejection over Hinnisdaels in view of Sobol, Isner, Vizard and Lundberg***

Claim 21 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Hinnisdaels in view of Sobol, Isner, Vizard and Lundberg. Applicants respectfully traverse this rejection.

A *prima facie* case of obviousness of claim 21 over Hinnisdaels in view of Sobol, Isner, Vizard and Lundberg has not been established. Nothing in these references would have motivated the skilled artisan to combine them to arrive at the claimed invention.

Claim 21 relates to compositions for nucleic acid manipulations, in which the reagents are at concentrations for performing the methods ***without dilution***, and wherein the composition has no nucleic acid molecules. Vizard discloses ***concentrates that are diluted*** prior to use. Thus, Vizard clearly teaches away from the present invention and cannot serve to create a *prima facie* case of obviousness.

In addition, claim 21 relates to compositions that ***lack nucleic acids*** and that can be stored for later use. Hinnisdaels, Isner and Lundberg disclose compositions that ***contain nucleic acids*** for immediate manipulation in their specific research. Thus, Hinnisdaels, Isner and Lundberg clearly teach away from the claimed invention and cannot serve to create a *prima facie* case of obviousness.

The remaining reference (i.e. Sobol) does not teach or suggest compositions for nucleic acid manipulation that comprise:

1. a nonionic detergent;
2. reagents, at concentrations for performing the methods without dilution;
3. a thermostable enzyme / polymerase which retains at least 90% of enzymatic activity for at least 4 weeks when stored at about 20-25°C; and
4. no nucleic acids.



Applicants therefore respectfully request that the rejection of claims 21 under 35 U.S.C. §103(a) over Hinnisdaels in view of Sobol, Isner, Vizard and Lundberg be reconsidered and withdrawn.

***K. Rejection over Heath in view of Sobol, Isner and Vizard***

Claims 1-2, 5, 8, 24-26, 28, 33, 40, and 48-49 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Heath in view of Sobol, Isner and Vizard. Claim 40 was previously cancelled, and claims 24, 25, 48 and 49 are sought to be cancelled without prejudice or disclaimer, so the rejection of these claims is moot. Applicants respectfully traverse this rejection with respect to remaining claims 1-2, 5, 8, 26, 28 and 33.

A *prima facie* case of obviousness of claims 1-2, 5, 8, 26, 28 and 33 over Heath in view of Sobol, Isner, and Vizard has not been established. Nothing in these references would have motivated the skilled artisan to combine them to arrive at the claimed invention.

Claims 1-2, 5, 8, 26, 28 and 33 relate to compositions for nucleic acid manipulations, in which the reagents are at concentrations for performing the methods ***without dilution***. Vizard discloses ***concentrates that are diluted*** prior to use. Thus, Vizard clearly teaches away from the present invention and cannot serve to create a *prima facie* case of obviousness.

In addition, claims 1-2, 5, 8, 26, 28 and 33 relates to compositions that ***lack nucleic acids*** and that can be stored for later use. Heath and Isner disclose compositions that ***contain nucleic acids*** for immediate manipulation in their specific research. Thus, Heath and Isner clearly teach away from the claimed invention and cannot serve to create a *prima facie* case of obviousness.

The remaining reference (i.e. Sobol) does not teach or suggest compositions for nucleic acid manipulation that comprise:

1. a nonionic detergent;
2. reagents, at concentrations for performing the methods without dilution;
3. a thermostable enzyme / polymerase which retains at least 90% of enzymatic activity for at least 4 weeks when stored at about 20-25°C; and
4. no nucleic acids.

Applicants therefore respectfully request that the rejection of claims 1-2, 5, 8, 26, 28 and 33 under 35 U.S.C. §103(a) over Heath in view of Sobol, Isner, and Vizard be reconsidered and withdrawn.

***Conclusion***

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request reconsideration and withdrawal of all presently outstanding rejections. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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